

REMARKS

The above amendments have been provided based on the format described at 1265 Off. Gaz. Pat. Office 87 (December 17, 2002) and as authorized by Deputy Commissioner for Patents, Stephen Kunin on January 31, 2003.

Claims 1-40 were pending, all of the claims were rejected in the previous Office action, and no claims were allowed. Claims 15-20 have been cancelled in light of business-related reasons and not in acquiescence to any rejection made by the Office. Claims 1, 22, and 23 have been amended in light of business-related reasons and not in acquiescence to any rejection made by the Office. Claims 1-14 and 21-40 are currently pending.

Invention

The invention relates to the use of prostate antigens or their representatives in vaccines to produce an immune response to prevent or treat cancer. While the prior art suggests the use of antigens uniquely associated with tumor tissue as components of antitumor vaccines, there is no suggestion to use antigens which are uniquely represented on host tissue for the tumor. Since the prostate is not an essential organ, elimination of the prostate gland, which may be a concomitant effect of the vaccines of the invention, does not adversely impact the general health of the subject. Thus, prostate cancer offers a unique opportunity for treatment with vaccines using antigens that characterize the host organ itself, rather than the malignant or metastatic nature of the cells *per se*.

Further, although it is recognized that prostate specific antigen (PSA) can be used in healthy experimental animals to generate antibodies for use in diagnosis, there is no suggestion that PSA or any other prostate antigen be used to elicit a protective or therapeutic immune response against prostate cancer.

References Filed with Appeal Brief and Admitted Evidence of May 7, 1998

Applicants respectfully submit that the Examiner has yet to substantively consider all of the references filed with the Appeal Brief or the declarations and references admitted on May 7,

1998. According to the Board of Patent Appeals and Interferences, “[w]hen an examiner allows new evidence into the record after the Notice of Appeal has been filed, he or she undertakes the responsibility to properly consider and complete the record as to his or her position why the evidence is not persuasive.” See bridging sentence on pages 4-5, Remand to the Examiner issued on January 31, 2001. Neither the declarations, accompanying experimental evidence, nor the references are addressed in the pending Action. Applicants are mystified as to the purpose of re-arguing what are essentially identical rejections from previous Actions. Moreover, Applicants believe the declarations and references of record provide objective evidence supporting the patentability of claims 1-14 and 21-40 and overcome the rejections set forth in this Action. Applicants address below the individual rejections in light of the declarations and references of record.

Rejection Under 35 U.S.C. § 112, First Paragraph - Written Description

Claims 1-14 and 21-40 are rejected under 35 U.S.C. § 112, first paragraph for reasons of record. Specifically, the Action maintains that there is insufficient guidance and direction as to the written description for “over represented antigens”, “nucleic acid sequences”, “proteins”, “peptides”, and “immunologically effective portion thereof.” The Action asserts that the DNA sequences of the claimed proteins and peptides are required, citing the Federal Circuit decision in *Fiers, Fiddes, and Eli Lilly*, and are not disclosed in the specification. Applicants respectfully traverse this rejection.

As previously noted in Paper 7 (filed November 22, 1994), the patentability of the instant invention lies not in the invention of prostate antigens or DNA sequences encoding prostate antigens, but rather in knowing what to do with the antigens. In other words, the patentability lies in the novelty of the method disclosed and not in the antigens.

1. Neither *Fiers, Fiddes*, nor *Eli Lilly* are applicable to the instant invention.

Fiers, Fiddes, and *Eli Lilly* are distinct from the instant invention because the claimed invention in each of these cases is a novel DNA sequence (*i.e.*, a composition claim). While

conception and reduction to practice of a novel DNA sequence requires the identification of the actual DNA sequence being claimed, it does not follow that the requirement for the recitation of DNA sequence is applicable to claims involving a method using proteins and DNA sequences where the patentability of the method lies in the method itself, not in a particular protein or DNA sequence. In fact, the Federal Circuit has recently affirmed that *Eli Lilly* does not hold that all functional descriptions of genetic material necessarily fail as a matter of law. *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 2003 U.S. App. LEXIS 118 (Fed. Cir. 2003). Rather the court looks to the knowledge in the art and whether the terms are such that an ordinary skilled artisan would comprehend the invention. Therefore, the requirement for a specific DNA sequence by the courts in *Fiers*, *Fiddes*, and *Eli Lilly* does not apply to the instant invention.

2. The specification as filed reasonably conveys possession of the claimed subject matter to one of skill in the art.

The subject matter of the claim need not be described literally (*i.e.*, using the same terms or in *in haec verba*) in order for the disclosure to satisfy the written description requirement. MPEP § 2163.02. The specification as filed complies with the standard articulated by the Federal Circuit for written description requirement. The instant specification discloses a genus of antigens useful in the claimed methods. These antigens are defined as over represented at page 5, lines 15-27. Immunologically effective portion of antigens useful in the claimed methods are specifically described at page 5, line 28 to page 6, line 3. A number of representative species of this genus of antigens are described in detail at page 7, line 12 to page 10, line 2. The specification also discloses detailed protocols for the preparation of these antigens at page 10, line 3 to page 12, line 19.

The evidence of record further supports the adequacy of the written description disclosed in the specification. In the declaration of Lynn Spitler submitted pursuant to 37 C.F.R. § 1.132 (submitted May 4, 1998), Spitler describes the use of one of the disclosed antigens, PSA, as well as various immunogenic PSA peptides *in vivo* and *in vitro* as described in the instant

specification. In sum, a skilled artisan would recognize Applicants had possession of the claimed invention based on the instant disclosure.

For the reasons stated above, the written description rejection under 35 U.S.C. § 112, first paragraph may be properly withdrawn.

Rejection Under 35 U.S.C. § 112, First Paragraph - Enablement

Claims 1-14 and 21-40 are rejected under 35 U.S.C. § 112, first paragraph for reasons of record. Applicants respectfully traverse this rejection for the reasons discussed below.

1. Objective evidence of record supports the sufficiency of the disclosure.

Applicants respectfully submit that the submission of objective evidence by the inventor and experts in the field of tumor immunotherapy on May 7, 1998 has not been properly considered. This evidence overwhelmingly demonstrates the *in vivo* operability of the claimed invention as well as the predictability of its efficacy. Applicants address below each of the concerns of the Office in light of the evidence submitted on May 7, 1998.

a. Over represented antigens serve as a therapeutic target for humans with prostate cancer.

Prostate specific antigen (*i.e.*, PSA) is disclosed as one species in the genus of over represented antigen in prostate cancer. *See* specification at page 8, line 18 to page 9, line 11. The declarations of Spitler report the results of five clinical trials using recombinant human PSA, which has been trademarked Onco Vax PTM. Antigen-specific T-cell responses were obtained in patients in all studies *in vivo* and *in vitro* with the patients in the fifth clinical study demonstrating dramatic and consistent T-cell responses. Dr. Spitler's declaration describes the status of the patients in the 5th clinical trial as all having undergone previous treatment, and three of the five patients having metastatic growth in the bone. Notably, in this patient cohort, all five patients evidenced a clinical response to the vaccine. In four of the five patients, the disease stabilized (*i.e.*, did not continue to grow), while one showed improvement (*i.e.*, improved bone

scan in patient 2). This is definitive evidence of the *in vivo* operability and predictability of the claimed invention.

b. *In vitro* and animal models of antitumor responses correlate with human efficacy.

Applicants respectfully submit that *in vitro* and animal models do correlate with *in vivo* clinical trial results submitted herein. Applicants have submitted publications of animal studies demonstrating the ability of a species of over represented antigens (*i.e.*, PSA) reduce tumor growth *in vivo* through the elicitation of an antitumor response. *See*, Wei, *et al.*, *Cancer Immunol. Immunother.* 42: 362 (1996). In fact, a murine antitumor response is also observed using the Onco Vax PTM itself. *See* Declaration of Dr. Gary Matyas (abstract entitled "Induction of Antitumor responses in Mice by Prostate Cancer Vaccine"). Moreover, Applicants have submitted *in vitro* and *in vivo* immunological responses gathered in initial patient cohorts that accurately predicts the *in vivo* responsiveness observed in the fifth trial with a different patient cohort. Applicants are unclear why the above evidence carries no weight with the Office and request additional clarification regarding the deficiencies of this evidence.

c. Results with the prostate vaccine of the instant invention are recognized as predictable by skilled artisans.

In vitro results, animal models, and *in vivo* immunologic responses are well known in the art as predictive of effective antitumor response *in vivo*. Contrary to the bald assertion made by the Office that the "antigenic or immunogenic nature of a protein ... does not necessarily correlate with its ability to confer antitumor responses," four experts in the field of tumor immunology state that "in my opinion, the results contained in [Spitler's] study provide evidence that the vaccines are likely to be effective in exerting a beneficial effect on patients with prostate tumors or at risk for prostate tumors" after a critical review of the evidence of record. Each of the experts also attests to the fact that the evidence generated by Spitler's trials indicates that "analogous vaccines based on host tissue antigens ... would behave in a similar manner." The experts - Michael Mastrangelo, Jean-Claude Bystry, Philip Livingston, and Robert Oldham -

are recognized by skilled artisans as pioneers in the field of tumor immunology and tumor vaccines. Each individual has successfully developed tumor vaccines and has published over 100 peer-reviewed publications in this area. Again, Applicants are perplexed as to why these declarations of skilled artisans in the relevant art carry no weight with the Office and are not even addressed in the Action.

2. The practice of the claimed invention does not require undue experimentation.

The enablement requirement of 35 U.S.C. § 112, first paragraph does not require a complete absence of experimentation in the practice of a claimed invention. In other words, routine experimentation does not constitute undue experimentation. *Johns Hopkins University v. Cellpro, Inc.*, 47 U.S.P.Q.2d 1705 (1998). The specification is only required to teach a skilled artisan how to make and use the invention.

a. The specification provides adequate guidance and working examples.

The specification teaches the skilled artisan how to make, formulate, and administer full-length antigens, immunologically reactive portions thereof, and nucleic acids encoding one or more of those antigens *in situ*. On page 10, line 9 to page 12, line 2, the specification teaches the skilled artisan how to prepare antigens. On page 12, lines 3-23, the specification teaches the skilled artisan how to generate immunologically effective portions of the antigens. Examples of generating the antigens *in situ* by an expression system are set forth on page 6, line 21 to page 7, line 14. On page 16, line 24 to page 17, line 4, the specification provides an example of a viral expression vector for the claimed nucleic acids, as well as disclosing "naked" DNA as useful in the claimed methods.

The specification also provides a description of compositions by which the claimed antigens may be formulated on page 14, line 15 to page 17, line 4. Furthermore, the specification on page 17, line 5 to page 19, line 20 provides the skilled artisan with a description of how to administer antigens and nucleic acids of the claimed methods.

Thus, one of ordinary skill in the art may practice the claim methods in view of the extensive teachings provided by the specification.

b. The evidence of record uses the guidance provided in the specification to elicit an effective antitumor response as demonstrated by Spitler.

The specification as filed provides all the guidance necessary for tumor vaccine demonstrated in the evidence submitted by Dr. Spitler. The expression system, a baculovirus system, is described at page 6, line 14 to page 7, line 6 and at page 11, lines 5-11 of the specification. Spitler uses one of the species in the claimed genus of over represented antigens on prostate cancer, namely PSA. PSA is disclosed at page 8, line 18 to page 9, line 11. The vaccine composition, *i.e.*, liposomes, is disclosed at page 14, lines 9-23 and at page 16, lines 13-18. The route of administration, *i.e.*, intramuscular, is disclosed at page 16, lines 1-3. The dose (100 µg) and volume (1 ml) administered is disclosed at page 16, lines 19-23. The sequential administration on a monthly basis is disclosed at page 16, lines 24-27 and at page 17, lines 8-12, respectively. Therefore, in every aspect of the clinical trial, Applicants relied on the guidance and examples provided in the specification as filed.

3. Spitler and Hodge provide credibility to the use of antitumor vaccines.

The Office action cites two documents, Spitler (*Cancer Biother.* 10:1-3 (1995)) and Hodge *et al.* (*Int. J. Cancer* 63:231-237 (1995)), which allegedly state the claimed methods would be unpredictable. Applicants respectfully submit that these documents demonstrate the credibility and the predictability of the claimed invention when read in their entirety.

In particular, Spitler states that

[I]nvestigators working in the university setting using vaccines to treat cancer patients have occasionally seen clinical responses to this therapy, which at times has been dramatic. Almost everyone working in this field has had the experience of seeing a dramatic regression of metastatic disease following vaccine therapy. There are numerous published reports of these responses as well as unpublished observations of individual investigators. (emphasis added)

While Spitler opines regarding the future of tumor vaccines, the Office has selected a single sentence that, in fact, mischaracterizes Spitler's point -- that active components of vaccines are

identified and purified and are now available for routine vaccine protocols. Hence, when read in its entirety, Spitler does not support the Examiner's contention that the successful use of antitumor vaccines would not be credible to a skilled practitioner or that undue experimentation is required to practice the claimed invention.

Hodge demonstrates the success of a human PSA vaccine in eliciting an antitumor response in an animal (*i.e.*, primate) model. Hodge reports a rhesus monkey study showing that a recombinant vaccinia virus that expresses human PSA successfully generates a humoral and cellular immune response without showing any toxicity. At page 236, Hodge states "we have shown that it is possible to mount humoral and cellular immune responses specific for PSA in rhesus monkey after immunization with a recombinant vaccinia virus expressing PSA." The Office has selected the statements characterizes tumor vaccines using whole cells – a fundamentally different vaccine protocol – and attributes them to the instant invention. In point of fact, the instant invention does not use or claim the used of whole cells to elicit an antitumor response. Therefore, one skilled in the art reading Hodge would be left with the conclusion that cell-based antitumor vaccines are not predictable as cancer vaccines. Because a skilled artisan understands that cellular vaccines and antigen vaccines are fundamentally different in the mechanisms by which an antitumor response is elicited, the statements of Hodge would not convey unpredictability for the use of the instant invention.

In summary, the two documents cited by the Examiner themselves support the position that a skilled artisan would not find the disclosure of the specification in any way incredible, that many antitumor vaccines have been tested and that the skilled artisan would have a reasonable expectation of success when practicing the teachings of the specification.

4. In light of the expert declarations and the evidence of record, Ezzell does not provide evidence of unpredictability.

As with Hodge, Ezzell addresses the limitations of tumor vaccines using cellular compositions. Moreover, Ezzell addresses the limitations of targeting a unique tumor antigen. As stated above, the instant invention is directed to over represented host antigens – not unique

tumor antigens. Therefore, problems typically associated with unique tumor antigens (*e.g.*, poor presentation on antigen presenting cells) are not present. Moreover, the evidence of record demonstrates the efficacy of the claimed approach. Hence, despite any prior failures, the tumor vaccine of the instant specification elicits an effective antitumor response.

5. Any experimentation is routine.

As described above, the specification provides extensive guidance and examples for practicing the claimed subject matter. In addition, the claimed methods have actually been shown to be effective for eliciting an immune response in patients using the guidance provided in the specification as filed. The teachings of the specification in conjunction with the efficacy of the claimed methods demonstrate that any experimentation required for practicing the claimed embodiments would not be undue.

The law allows for the level of repetition required for practicing the claimed methods. For example, in *In re Wands*, 8 USPQ.2d 1400 (Fed. Cir. 1988), the Court of Appeals for the Federal Circuit found that a claim reciting the use of any high affinity IgM was fully enabled despite the fact that the claim read on the use of nearly an infinite number of particular antibodies. While it would require an enormous amount of effort to practice every embodiment, only a minimal amount was required to practice any one embodiment. In other words, if the experimentation required is only the use of well known and conventional methods, the experimentation is not undue simply because some experimentation is required.

The specification teaches all of the steps required for practicing the proven claimed invention, and all that remains is repetition of these teachings to practice the scope of the claims. As described above, the claimed methods have been carried-out according to the teachings of the specification using PSA as an antigen and result in an effective antitumor immune response. Repeating vaccine studies for different antigens, including full-length polypeptides, portions of those polypeptides, and nucleic acids that express the foregoing polypeptides *in situ*, is routine. The routine nature of identifying and using immunogenic peptide is confirmed by each of the experts in the declarations of record. Thus, the claimed methods can be easily practiced by a

person of ordinary skill in the art with only routine experimentation. Accordingly, any experimentation required for practicing the claimed methods would not be undue.

For the reasons stated above, the rejection under 35 U.S.C. § 112, first paragraph may be properly withdrawn.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 1-2, 4-8, 10-14, 21-22, 24-28, 30-34, and 37-40 are rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite in the recitation of "over represented antigens". Applicants respectfully traverse this rejection.

The instant specification contains an express teaching of what constitutes an over represented antigen at page 5, lines 15-27 using well known and conventional assessments of therapeutic toxicity. Moreover, the interpretation of the PSA results by the experts cited above indicates that these skilled artisans understood that other antigens like PSA (*i.e.*, over represented in prostate cancer) would behave similarly. Thus, skilled artisans would understand the metes and bounds of the instant claims.

For the reasons stated above, the rejection under 35 U.S.C. § 112, second paragraph may be properly withdrawn.

Rejection Under 35 U.S.C. § 103(a)

Claims 1-14 and 21-40 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Spitler in view of Israeli, Horoszewicz, Andriole *et al.*, and in view of art acknowledged methods of delivering antigens of interest to stimulate antitumor responses, as disclosed on pages 10-19 of the instant specification and in further evidence of McCarley *et al.* Applicants traverse this rejection for reasons of record and for the additional reasons discussed below.

Applicants respectfully submit that a *prima facie* case for obviousness has not been presented. The claimed methods relate to the use of overrepresented prostate antigens to induce an antitumor response in a subject. Therefore, a *prima facie* case of obviousness requires that the

cited combination of references result in the use of overrepresented prostate antigens to induce an antitumor response in a subject. The combination of cited references must provide a motivation to combine the teachings of these references to result in the claimed methods, and most importantly, the references must provide a reasonable expectation of success in combining these teachings. *Manual of Patent Examination Procedure* § 2142 (8th ed. 2001).

1. The cited documents do not result in the claimed methods.

Applicants respectfully submit that the combination of the cited references do not result in the claimed methods because the references do not teach or suggest the use of overrepresented prostate antigens in a subject to elicit an antitumor response. The Office seems to rely on the assumption that a demonstration that any one tumor antigen can elicit an immune response of any kind results in the claimed methods using overrepresented prostate antigens to elicit an anti-prostate tumor response. Applicants submit that this point of view is not supported by Spitler, the other cited references, what is known in the art or any combination thereof.

a. All tumor antigens are not alike.

A careful reading of Spitler reveals its failure to teach or suggest the use of overrepresented prostate antigens to elicit an antitumor response in a subject, a point as yet unappreciated by the Office. In its reliance on Spitler, the Office seems to be asserting that antigens uniquely associated with the transformed cell phenotype are equivalent to overrepresented prostate-specific antigens. The claimed methods use antigens that are organ-specific antigens, expressed solely on normal prostate tissue and prostate tumor tissue, and thus are not uniquely associated with the malignant nature of the prostate cells or other tumor cells. Spitler, on the other hand, teaches the use of antigens that are uniquely associated with the malignant or metastatic nature of the cells. Specifically, Spitler discloses the use of only two antigens (*i.e.*, CO-029 and GA733-2) that are each characterized by expression on multiple types of malignant cells. *See* Spitler, at column 2, lines 22-26. Thus, the claimed methods are distinct from Spitler in the choice of antigen. The antigens selected are characterized as being expressed on a variety of tumors, not any particular tumor or tissue. In other words, Spitler teaches the use

of a pan-epitope to stimulate a general antitumor immune response against any malignant cell. This is distinct from the use of discrete organ-specific antigens used as tumor antigens to elicit an anti-prostate tumor response of the instant claims. Thus, contrary to the assertions of the Office, Spitler does not teach the use of organ-specific antigens in vaccine compositions and methods.

b. Active immunotherapy is separate and distinct from passive immunotherapy.

The instant claims relate to a method using PAP and PSMA in active immunotherapy. While Israeli, Horoszewicz, and McCarley disclose prostate antigens, neither reference teaches nor suggests the use of an antigen to elicit an active antitumor immune response. Here the Office appears to equate active and passive immunotherapy. Applicants respectfully submit that these immunotherapies are distinct and non-overlapping therapies with distinct antigen requirements. Active immunotherapy requires the administration of an antigen that then induces the host immune system to produce antibodies and/or T cells specific for that antigen that can effectively remove the antigen (and its source). Passive immunotherapy, on the other hand, requires nothing from the host immune system. The host is the recipient of an agent, typically an antigen-specific antibody derived from another source (*e.g.*, tissue culture, mice, etc.), that mediates its antitumor activity with little or no participation from the host immune system. Israeli teaches the use of PSMA in passive immunotherapy of tumors. *See* Israeli, at column 12, line 53 to column 13, line 9. Active immunotherapy is not mentioned. Similarly, Horoszewicz teaches the use of prostate antigen-specific antibodies for passive immunotherapy. Horoszewicz's only disclosure of an active immunotherapy protocol does not employ antigen, but uses anti-idiotypic antibodies, a fundamentally different therapy (*i.e.*, antigen administration is never required). *See* Horoszewicz, at column 12, lines 21-29. McCarley also has no teaching or suggestion regarding the use of prostate antigens in active immunotherapy. McCarley's teachings are limited to the disclosure of a number of monoclonal antibodies that bind various prostate antigens and may be useful for passive immunotherapy (*e.g.*, when conjugated to a chemotherapeutic agent).

Therefore, if these references are to be relevant to the claimed methods, it must be assumed that the ability to elicit antigen-specific antibodies in non-tumor bearing animals is equivalent to eliciting an effective antitumor response in a subject. Such an assumption cannot be supported scientifically. It is well known in the art the immunogenicity required to elicit specific antibodies that simply bind an antigen does not correlate with, and is often distinct from the ability to elicit an effective antitumor response, whether humoral or cellular. Thus, these references do not cure the deficiencies in the Spitler reference.

Andriole *et al.* has no teaching or suggestion regarding the use of prostate antigens to elicit an antitumor response, and thus is not properly prior art.

In sum, the combination of references cited by the Office do not teach or suggest the use of overrepresented prostate antigens in active tumor immunotherapy.

2. There is no suggestion or motivation to combine the cited references.

The cited documents provide no suggestion or motivation to combine the teachings to elicit an immune response using antigens expressed in normal prostate tissue. Of all of the references cited by the Office, only Spitler discloses active immunotherapy using tumor antigens. Because passive and active immunotherapy are functionally and mechanistically distinct, a skilled artisan would have no motivation to combine Spitler with the disclosures teaching passive immunotherapy in Israeli, Horoszewicz, or McCarley.

In fact, Spitler teaches away from the claimed methods. Spitler teaches the need for a vaccine that is “efficacious in the prevention and treatment of all cancers.” Spitler, at column 1, lines 50-51 (emphasis added). Spitler also teaches that the disclosed compositions are those useful “for the prevention and treatment of a variety of cancers.” Spitler, at column 2, lines 19-21 (emphasis added). In order for such a vaccine to be effective and non-toxic, the target antigen would not be one expressed on normal tissue. A skilled artisan would recognize that the administration of a prophylactic vaccine that elicits an immune response to an antigen on normal tissues would result in autoimmunity specific for that tissue, a potentially fatal side effect. Alternatively stated, Spitler’s teachings require the use of antigens that are not expressed on

normal tissues to achieve its intended purpose. Hence, nothing in Spitler teaches the extension of its teachings to antigens expressed in an organ-specific manner in normal tissues alone or in any combination with the references cited by the Office.

Because the modification of Spitler's teachings to include organ-specific antigens expressed on normal tissues would render the vaccine unsatisfactory for its intended purpose (*i.e.*, prophylactic and therapeutic vaccine), there is no motivation or suggestion to make such a modification. MPEP § 2143.01 at page 2100-124, second column ("if the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification") (citations omitted).

3. The combination of cited references fail to provide a reasonable expectation of success for the claimed methods.

Finally, the references do not provide a reasonable expectation of success in any combination. The majority of the references do not even address active immunotherapy, thus making it impossible for them to convey any expectation of success. Spitler's teaching of active immunotherapy suggests that the use of organ-specific antigens that are also expressed on normal tissues are not candidates for tumor active immunotherapy, thus teaching that such an approach would not be successful.

For the reasons stated above, the rejection under 35 U.S.C. § 103(a) may be properly withdrawn.

Rejection for Alleged Obviousness-Type Double-Patenting

Claims 1-14 and 21-40 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-8 of U.S. Patent No. 5,925,362. Applicants respectfully request that this rejection be held in abeyance until the above-identified issues have been resolved.

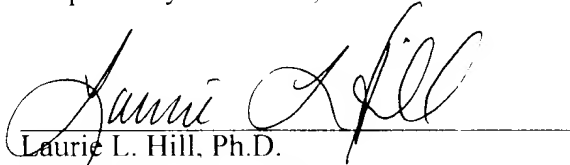
CONCLUSION

Applicants submit that the rejection under 35 U.S.C. §§ 112 and 103 have been overcome by the above remarks. Early allowance of pending claims 1-14 and 21-40 is respectfully requested. In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 204372000300.

Respectfully submitted,

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